research

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ORIGINAL RESEARCH Retrospective cohort study

Delirium and incident dementia in hospital patients in New South Wales, Australia

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Study question To what extent does delirium increase the risk of a new dementia diagnosis in older adult patients?

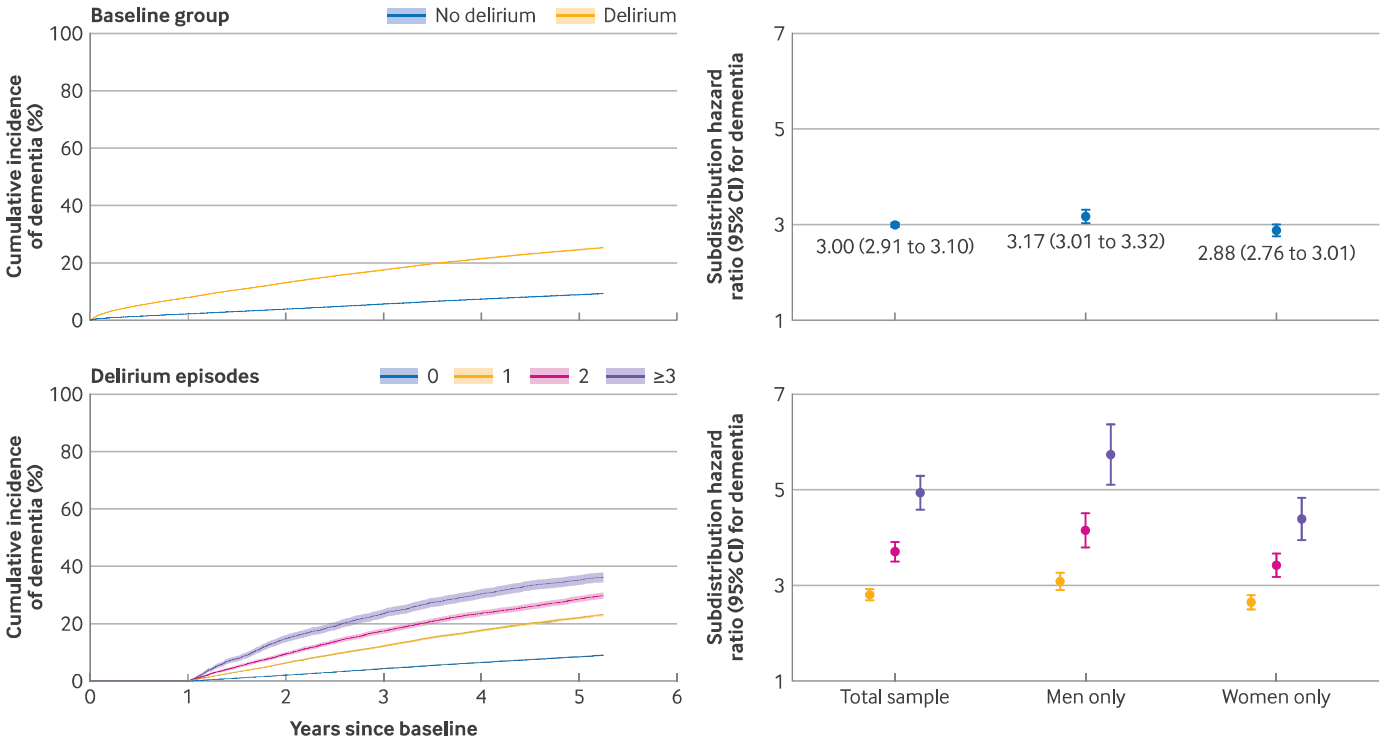
Methods Data were extracted from an administrative dataset for 650 590 patients aged 65 years and older who were admitted to private and public hospitals in New South Wales, Australia between July 2001 and March 2020. Diagnoses of dementia and delirium were identified from ICD-10 (international classification of diseases, 10th revision) codes. Patients with dementia at baseline were excluded. Patients with delirium were matched 1:1 to patients without delirium according to patient and episode characteristics, and they were followed for more than five years. Cox proportional hazard models and Fine-Gray hazard models were used to estimate the associations of delirium with death and incident dementia, respectively. Analyses were performed in men and women separately.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- An association might exist between delirium and subsequent dementia; however, the strength and nature of this association are unclear because of limitations in existing observational studies
- As the global burden of dementia increases, it is important to confirm the extent to which delirium is a potentially modifiable risk factor

WHAT THIS STUDY ADDS

- Among patients without dementia at baseline with at least one episode of delirium, the risk of a new dementia diagnosis was about three times higher than for patients without delirium; each additional episode of delirium increased the risk by 20%
- The association between delirium and incident dementia seems to be stronger in men than in women
- The prevention and treatment of delirium could reduce the burden of dementia globally



Association of delirium with incident dementia by baseline group (upper panel) and episodes of delirium recorded within first 12 months of follow-up (landmark period; lower panel). Associations presented in forest plot in lower panel were adjusted for age and gender at baseline, and number of hospital episodes recorded within landmark period. Total sample data are subdistribution hazard ratio 2.81 (95% confidence interval 2.70 to 2.92) for one delirium episode, 3.70 (3.50 to 3.91) for two episodes, and 4.91 (4.57 to 5.28) for three or more episodes. Corresponding data for men only are 3.06 (2.88 to 3.25), 4.15 (3.81 to 4.52), and 5.72 (5.12 to 6.38). Corresponding data for women only are 2.64 (2.51 to 2.78), 3.42 (3.18 to 3.67), and 4.39 (3.99 to 4.83)

Study answer and limitations The study included 55 211 matched pairs (48% men, mean age 83.4 years, standard deviation 6.5 years). Collectively, 58% (n=63 929) of patients died and 17% (n=19 117) had a newly reported dementia diagnosis during 5.25 years of follow-up. Patients with delirium had a 39% higher risk of death (hazard ratio 1.39, 95% confidence interval (CI) 1.37 to 1.41) and three times higher risk of incident dementia (subdistribution hazard ratio 3.00, 95% CI 2.91 to 3.10) than patients without delirium. Among patients with at least one episode of delirium, each additional episode increased the risk of dementia by 20%. The association between delirium and dementia was stronger in men. A key limitation of the study was the dependence upon clinical coding of diagnoses in the administrative dataset.

What this study adds Delirium appears to increase the risk of dementia threefold among older hospital patients, and there could be a causal link between the two conditions.

Funding, competing interests, and data sharing
Supported by the National Health and Medical Research Council: Partnership Centre for Health System Sustainability. No competing interests declared. Data are available on application to data repository, and data analysis scripts can be downloaded.

LISA MAREE WILLIAMS/GETTY IMAGES

Derivation and external validation of a simple risk score for predicting severe acute kidney injury after intravenous cisplatin

Gupta S, Glezerman IG, Hirsch JS, et al

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Study question What are the risk factors for cisplatin associated acute kidney injury, and is this type of acute kidney injury associated with a higher risk of death?

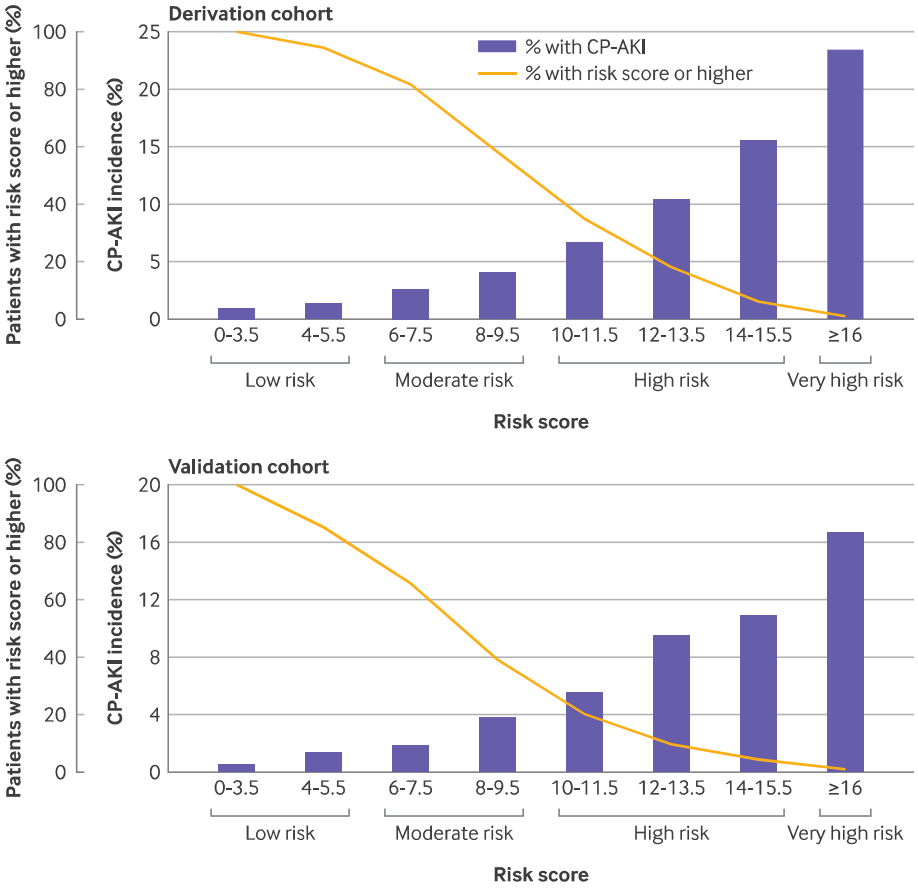
Methods The study population comprised adults (≥18 years) receiving their first dose of intravenous cisplatin during 2006-22 at six geographically diverse major academic cancer centres across the US. The primary outcome was cisplatin associated acute kidney injury, defined as a twofold or more increase in serum creatinine level or kidney replacement therapy within 14 days of a first dose of intravenous cisplatin. Risk factors for cisplatin associated acute kidney injury were identified in a derivation cohort and tested in an external validation cohort. The association between cisplatin associated acute kidney injury and survival was also examined.

Study answer and limitations A total of 24 717 adults were included, with 11 766 in the derivation cohort (median age 59 (interquartile range (IQR) 50-67)) and 12 951 in the validation cohort (median age 60 (IQR 50-67)). The incidence of cisplatin associated acute kidney injury was 5.2% (608/11 766) in the derivation cohort and 3.3% (421/12 951) in the validation cohort. Each of the following factors were independently associated with cisplatin associated acute kidney injury in the derivation cohort: age, hypertension, diabetes mellitus, serum creatinine level, haemoglobin level, white blood cell count, platelet count, serum albumin level, serum magnesium level, and cisplatin dose. Compared with patients in the lowest risk category, those in the highest risk category showed a 24-fold (95% confidence interval 13.49 to 42.78) higher odds of cisplatin associated acute kidney injury in the derivation cohort and a 17.87-fold (10.56 to 29.60) higher odds in the validation cohort. Greater severity of cisplatin associated acute kidney injury was associated with shorter 90 day survival. Limitations of the study included lack of data on medications used at home and that the study only included US based centres.

What this study adds This study found that a simple risk score based on readily available variables from patients receiving intravenous cisplatin could predict the risk of severe cisplatin associated acute kidney injury, the occurrence of which is strongly associated with death.

Funding, competing interests, and data sharing
No funding received. See full paper on bmj.com for competing interests. No additional data available.

Risk factor	Odds ratio (95% CI)	Score
Age (years)		
≤45	1 (reference)	0
46-60	2.90 (2.06 to 4.09)	2.5
61-70	4.12 (2.91 to 5.83)	3.5
>70	5.15 (3.49 to 7.60)	4.5
Hypertension	1.31 (1.09 to 1.58)	1
Diabetes	1.30 (1.02 to 1.64)	1
Current/former smoker	1.20 (1.00 to 1.45)	1
Haemoglobin (g/L)		
≥120	1 (reference)	0
110-119	1.41 (1.10 to 1.82)	1
<110	1.62 (1.28 to 2.05)	1.5
White blood cell count (x10^9/L)		
≤12.0	1 (reference)	0
>12.0	1.59 (1.25 to 2.02)	1.5
Serum albumin (g/L)		
>38	1 (reference)	0
33-38	1.28 (1.01 to 1.62)	1
<33	1.73 (1.30 to 2.29)	1.5
Serum magnesium (mmol/L)		
≥0.82	1 (reference)	0
<0.82	1.39 (1.14 to 1.70)	1
Cisplatin dose (mg)		
≤50	1 (reference)	0
51-75	2.16 (1.47 to 3.18)	2
76-100	3.19 (2.10 to 4.84)	2.5
101-125	3.41 (2.14 to 5.44)	3
126-150	6.40 (4.29 to 9.53)	5
151-200	8.81 (5.99 to 12.94)	7.5
>200	11.74 (7.68 to 17.94)	9.5



Risk factors for CP-AKI in the simple risk model, and incidence of CP-AKI according to risk score in the derivation and validation cohorts. Left panel shows the risk factors for CP-AKI in the simple risk model, along with their odds ratios and associated score points. Top right and bottom right panels show the incidence of CP-AKI in the derivation and validation cohorts, respectively, according to risk score. CI=confidence interval; CP-AKI=cisplatin associated acute kidney injury

Use of progestogens and the risk of intracranial meningioma

Roland N, Neumann A, Hoisnard L, et al

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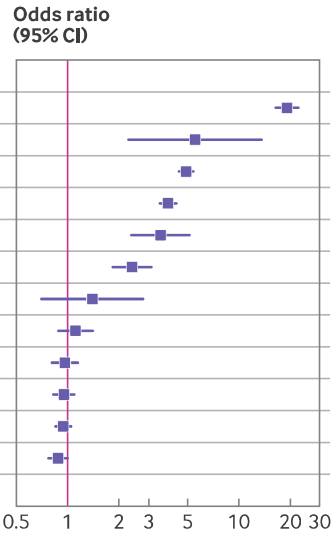
Study question What is the risk of intracranial meningioma associated with the use of selected progestogens?

Methods Using data from the French national healthcare database (Système National des Données de Santé), 18 061 women who were admitted to hospital for intracranial surgery for meningioma between 1 January 2009 and 31 December 2018 were compared with 90 305 women with no history of meningiomas (case-control study). Previous use of progestogens (progesterone, hydroxyprogesterone, dydrogesterone, medrogestone, medroxyprogesterone acetate, promegestone, dienogest, or levonorgestrel by intrauterine systems) in both groups were compared and each association between progestogen and meningioma was analysed using conditional regression (odds ratio). For each progestogen, use was defined by at least one dispensation within the year before the index date (within three years for 13.5 mg levonorgestrel intrauterine systems and five years for 52 mg). Five women in the control group were randomly matched to each woman in the case group for the year of birth and area of residence. Women who were pregnant in the two years preceding the index date were excluded.

Study answer and limitations Mean age was 57.6 years (standard deviation 12.8). Prolonged use of at least one year of medrogestone, medroxyprogesterone acetate, and promegestone was found to increase the risk of intracranial meningioma: for medrogestone, 42 exposed cases/18 061 cases (0.2%) *v* 79 exposed controls/90 305 controls (0.1%), odds ratio 3.49 (95% confidence interval (CI) 2.38 to 5.10), for medroxyprogesterone acetate (injectable, 9/18 061 (0.05%) *v* 11/90 305 (0.01%), 5.55 (2.27 to 13.56)), and for promegestone (83/18 061 (0.5%) *v* 225/90 305 (0.2%), 2.39 (1.85 to 3.09)). No excess risk was found for intracranial meningioma for progesterone, dydrogesterone, or levonorgestrel intrauterine systems. A highly increased risk of meningioma was observed for cyproterone acetate (891/18 061 (4.9%) *v* 256/90 305 (0.3%), odds ratio 19.21 (95% CI 16.61 to 22.22)), nomegestrol acetate (925/18 061 (5.1%) *v* 1121/90 305 (1.2%), 4.93 (4.50 to 5.41)), and chlormadinone acetate (628/18 061 (3.5%) *v* 946/90 305 (1.0%), 3.87 (3.48 to 4.30)), which were used as positive controls for use. Further studies are needed concerning dienogest or hydroxyprogesterone because no conclusions could be drawn from this study given the small number of individuals who had used these drugs.

What this study adds The increased risk associated with the use of injectable medroxyprogesterone acetate, a widely used contraceptive, and the safety of levonorgestrel intrauterine systems are important new findings. Although the risk of meningioma was already known for three progestogens (chlormadinone acetate, nomegestrol acetate, and cyproterone acetate), this study assessed the risk associated with progestogens that are much more widely used for multiple indications, such as contraception.

	Case group (%) (n=18 061)	Control group (%) (n=190 305)
Cyproterone acetate	891 (4.9)	256 (0.3)
Medroxyprogesterone acetate	9 (0.05)	11 (0.01)
Nomegestrol acetate	925 (5.1)	1121 (1.2)
Chlormadinone acetate	628 (3.5)	946 (1.0)
Medrogestone	42 (0.2)	79 (0.1)
Promegestone	83 (0.5)	225 (0.2)
13.5 mg LNG intrauterine system*	10 (0.2)	48 (0.2)
Percutaneous progesterone	90 (0.5)	503 (0.6)
Dydrogesterone	156 (0.9)	990 (1.1)
Spironolactone	264 (1.5)	1473 (1.6)
52 mg LNG intrauterine system*	566 (3.7)	3888 (5.1)
Oral and intravaginal progesterone	329 (1.8)	2149 (2.4)



Associations between various progestogens and risk of intracranial meningioma requiring surgery (odds ratio in logarithmic scale). CI=confidence interval; LNG=levonorgestrel. *LNG had different denominators due to restricted inclusion periods (10/4048 cases, 48/20 240 controls; 566/15 162 cases, 3888/75 810 controls)

WAVEBREAK MEDIA PREMIUM/ALAMY

Funding, competing interests, and data sharing
This research was funded by the French National Health Insurance Fund (Cnam) and the French National Agency for Medicines and Health Products Safety (ANSM). No competing interests declared. Under the terms of the SNDS data use agreement, the complete study data cannot be shared with other investigators (www.snds.gouv.fr). Algorithms and other additional information are in the supplemental data; aggregated data can be supplied by the corresponding author at noemie.roland@assurance-maladie.fr.